REMARKS

Claims 1, 4-11, 15-30 and 56 are currently pending in this application. Claims 22-30 have been withdrawn from further consideration by the Examiner as being drawn to a non-elected invention. The specification has been amended to replace the Title. Claims 1, 6, 11, 18, and 27 have been amended, and new claims 57-62 have been added. No new matter has been added by way of this amendment, and support can be found in the specification, *e.g.*, at page 17, lines 26-31 and in original claims 1, 6, 18 and 27.

Following entry of this amendment, claims 1, 4-11, 15-21, and 56-62 will be pending. Applicants respectfully request reconsideration of pending claims 1, 4-11, 15-21 and 56-62.

The Examiner has acknowledged consideration of references cited in the Information Disclosure Statements and Forms 1449 filed on October 27, 2003; August 29, 2005; and September 15, 2005. In addition, Applicants respectfully request acknowledgement of the Supplemental Information Disclosure Statement and references cited on Form 1449 filed on March 7, 2005.

Also, an Official Filing Receipt was never received by the Applicants. Thus, Applicants respectfully request that an Official Filing Receipt be sent as soon as possible.

I. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 6, 7, and 18 have been rejected by the Examiner under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for the recitations of "CM," "a natural biological cell adhesion agent," and a "synthetic biological cell adhesion agent" (Office Action, pages 2-3).

Applicants respectfully traverse this ground of rejection.

Only a "reasonable degree of particularity and distinctness" is required to satisfy 35 U.S.C. § 112, second paragraph, and that "[s]ome latitude in the manner of expression and the

aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire" (Manual of Patent Examining Procedure, 8th Ed., Incorporating Revision No. 4 (2006) ("M.P.E.P.") § 2173.02).

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.
>
> In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. *See, e.g., Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000)....See also *Metabolite Labs., Inc. v. Lab Corp of America Holdings*, 370 F.3d 1354, 1366, 71 USPQ2d1081, 1089 (Fed. Cir. 2004 ("Te requirement to 'distinctly' claim means that the claim must have meaning discernable to one of ordinary skill in the art when construed according to correct principles....Only when a claim remains insolubly ambiguous without a discernable meaning after all reasonable attempts at construction must a court declare it indefinite.").

Id. (Emphasis added).

Applicants respectfully submit that the recitation of "CM dextran" in claims 6, 7, and 18 is clear and unambiguous. As appreciated by those skilled in the art, "CM dextran" is an abbreviation for a CarboxyMethyl derivative of the dextran polysaccharide (*see, e.g.*, Appendix A).

However, solely in an effort to advance prosecution of this application, Applicants have amended claim 6 to recite "carboxymethyl (CM) dextran." No new matter has been added by way of this amendment.

Applicants further submit that "biological cell adhesion agents" and "synthetic cell adhesion agent" is clear and unambiguous. As those skilled in the art are aware, cell adhesion agents or promoters are materials that promote or enhance the adhesiveness of cells (*e.g.*, to other cells or the surface of the microspheres) or to form a "bridge" between living cells and a substrate (*e.g.*, the microsphere). As those skilled in the art are aware, a number of biological cell adhesion agents are available for use with the invention, such as, for example, fibronectin, vitronectin, *etc.* Additionally, as those skilled in the art will appreciate, "synthetic" cell adhesion agents--as the name implies--are those formed by synthetic processes, such as, for example, recombinant technologies.

However, solely in an effort to advance prosecution of this application, Applicants have amended claims 6 and 18 to delete the phrase "biological cell adhesion agent and a synthetic cell adhesion agent." Instead, Applicants have added new claims, which recite that the cell adhesion promoter is a natural biological cell adhesion promoter (claims 57 and 59) or a synthetic biological cell adhesion promoter (claims 58 and 60). No new matter has been added by way of this amendment, nor has the scope of the claims been narrowed, and support can be found in the paragraph corresponding to [0032] in U.S. Publication No. 2004/0091425 (PTO publication of the above-referenced application) and original claims 6, 18 and 27.

Thus, for at least the reasons above, Applicants submit that claims 6, 7 and 18 (as well as new claims 57-62) comply with all the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

II. Rejection Under 35 U.S.C. § 103

A. Bachtsi *et al.*

Claims 1, 4-6, 11, 15-18 and 56 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Bachtsi *et al.* (1995) *J. Microencapsulation,* 12:23-25 ("Bachtsi") (Office Action, page 3-4).

Applicants respectfully traverse this ground of rejection.

The Examiner cites Bachtsi as disclosing spherical crosslinked PVA particles that range in size from 30-80 μm, which were placed in a protease enzyme solution for loading (Office Action, pages 3-4). While the Examiner acknowledges that Bachtsi fail to teach sterile microspheres, the Examiner opines that it would have been obvious to modify the microspheres of Bachtsi to generate sterile microspheres because Bachtsi discloses that crosslinked PVA hydrogel matrices may be used as drug delivery systems (*Id.* at page 4).

However, contrary to the Examiner's assertions, it would not have been obvious to modify the microspheres of Bachtsi to produce microspheres useful for embolization wherein said microspheres comprise crosslinked polyvinylalcohol where said microspheres (a) have a diameter ranging from about 10 μm to about 2,000 μm, (b) are substantially spherical, (c) are substantially uniform in size and shape, (d) are sterile and (e) are in the form of a dry powder.

Although Bachtsi mentions that hydrogels may be used as "controlled delivery devices of various biomolecules, including drugs, enzymes, and antibodies," it is mentioned solely in the context of the introductory background section (*see* Bachtsi discussing prior art on the paragraphs spanning pages 23-24). The remainder of the Bachtsi article discusses the "use of crosslinked poly(vinyl alcohol) hydrogel particles as controlled delivery devices for enzymes" (Bachtsi, paragraph spanning pages 23-24).

A mere "suggestion may make an approach 'obvious to try' but it does not make the invention obvious."

> *Ex parte Obukowicz*, 27 USPQ2d 1063, 1065 (Bd. Pat. App. & Int'f 1992) (claim to insect combating method comprising applying to a plant environment or seed plant-colonizing bacteria that (1) have in its chromosome heterologous DNA encoding for *Bacillus thuringiensis* protein toxin, and (2) are capable of proliferating in the environment and expressing the toxin; the Examiner rejected the claim as obvious in view of a reference that discussed incorporating the toxin-encoding gene in bacteria, contained little information on how to use the transformed bacteria, and suggested that the gene be transferred into "other bacteria which have better survival in nature"; HELD: the Examiner erred in finding that the cited reference provided the "suggestion" for combination that case law requires; "At best, the [reference's] statement is but an invitation to scientists to explore a new technology that seems a promising field of experimentation. The...statement is of the type that gives only general guidance and is not at all specific as to the particular form of the claimed invention and how to achieve it. Such a suggestion may make an approach 'obvious to try' but it does not make the invention obvious."; the reference suggestion may have referred to an approach different from that claimed: inclusion of the toxin gene in pond surface flourishing cyanobacteria).

Chisum on Patents Vol. 2, section 5.04(8)(d) (Release No. 82, December 2002) (emphasis added).

Thus, while it is true that Bachtsi discloses in introductory remarks that hydrogels had been used in the past for drug, enzyme and antibody delivery, the reference does not teach or make obvious the claimed invention. These statements, at best, are only an invitation to explore hydrogels in the context of drug delivery. The statement gives no guidance whatsoever as to what to what properties the hydrogels should have or in what fields to explore the use of hydrogels. Further, these statements are in no way specific as to the particular form of the instantly claimed microspheres, which comprise crosslinked polyvinylalcohol, wherein said microspheres (a) have a diameter ranging from about 10 μm to about 2,000 μm, (b) are substantially spherical, (c) are substantially uniform in size and shape, (d) are sterile and (e) are in the form of a dry powder.

Moreover, the mere fact that "hydrogels" existed in the prior art as enzyme, drug, and antibody delivery systems, does not lead one to conclude that the microspheres of Bachtsi should be modified to be sterile and/or would be useful in the field of vascular embolization.

As those skilled in the art are aware, many drug application forms do not require sterile ingredients. For example, pills, ointments, nasal drops, *etc.*, are kept in a clean environment, but do not necessarily have to be sterilized, and tend to be applied or ingested in a non-sterile environment.

Additionally, the subject matter of Bachtsi is concerned with release properties of enzyme-loaded PVA microspheres. The ultimate purpose for studying the enzyme release properties of the microspheres is unknown. In fact, the only assays used to determine enzyme-release activity of the microspheres in Bachtsi is a "milk enzyme assay":

> The principle of the milk test used for the determination of the activity of protease enzymes is based on the cleaving of the milk caseins by the enzymes. The time elapsed from the addition of the enzymes to the milk until the start of the coagulation can be related to the enzyme activity. Thus, the lower the enzyme activity, the longer will be the time for the coagulation of the milk. By measuring the cleaving time of the enzymes before and after the soaking process, one can determine the residual enzyme activity, as well as the efficacy of the enzyme entrapment process.

(Bachtsi, page 28, first full paragraph; emphasis added). The "milk test" described above indicates use of the microparticles in the food industry as opposed to the pharmaceutical industry. Nowhere do the authors disclose or suggest that theses enzyme-loaded microspheres would be suitable for (1) any pharmaceutical composition, (2) any medical treatment generally, (3) for vascular embolization specifically, and/or (4) any patient population whatsoever, *much less* that the particles should be sterile, as recited in the claims.

For at least these reasons, Applicants submit that the claims are non-obvious over Bachtsi. Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

B. Barnes *et al.*

Claims 1, 8, 9, 11, 19 and 20 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Barnes *et al.* (1999) *Cytometry,* 36:169-175 ("Barnes") (Office

Action, page 4-5).

Applicants respectfully traverse this ground of rejection.

Barnes was published online on June 15, 1999. The above-reference application was filed on October 27, 2003 and is a continuation of U.S. Serial No. 09/419,114 filed October 15, 1999 (now U.S. patent No. 6,680,046), which claims priority to FR Application Serial No. 98-13019 filed October 16, 1998.

Thus, because Barnes was not published prior to the date of invention, Barnes is not a proper prior art reference under 35 U.S.C. §§ 102(a) and/or 103(a). Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

III. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully submit that this application is now in condition for immediate allowance. If the Examiner disagrees, Applicants respectfully request that the Examiner call the undersigned at the number listed below.

A Petition for a One (1) Month Extension of Time, including provisions for the required fee, is submitted herewith, which extends the response period from February 16, 2006 to, and including, March 16, 2006.

Applicants believe no other fees are due in connection with this response. However, if there are any fees due, please charge them to Deposit Account 50-3013. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above or in the Petition filed concurrently herewith, such an extension is requested and the fee should be charged to

our Deposit Account. Also, please charge any fees underpaid or credit any fees overpaid to the same Deposit Account.

Respectfully submitted,

Date: Mar. 16, 2006

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